whether or not cardiac local RAS abnormality caused by AT1-AA contributes to fetal rat ventricular hypertrophy.
Methods: To establish AT1-AA-positive pregnant rat model, AT1-AA was purified from preeclamptic patients and the pregnant rats was given a tail vein injection of AT1-AA on 13, 15 days of gestation. The myocardial cell morphology changes were detected by HE staining. The fetal rat heart heavy weight/body weight ratio was calculated. The expressions of Ang II and AT1R in the fetal cardiac tissue were detected by radioimmunoassay and immunohistochemical techniques, respectively. The AT1R expressions in culture myocardial cells were determined by western blot.
Results: The titer of the serum AT1-AA were significantly higher (0.288± 0.096 vs. 0.112 ±0.058, $P<0.01$ vs control group) and the systolic blood pressure was increased in AT1-AA positive pregnant rats (136±12mmHg *vs.* 101± 4mmHg, $P<0.05$, *vs.* control group). Left ventricular wall was thickened and diameter of cardiomyocytes was increased in the AT1-AA positive fetal heart at late pregnancy (18 days), while the high expression of AT1R ($P<0.05$) and significantly increased local Ang II (1320±256pg/ml vs498±124 pg/ml, $P<0.05$, *vs.* control group) were detected in fetal myocardial tissue. Additionally, the expression of AT1R in cultured myocardial cell membrane of fetal rat was increased after incubated with AT1 - AA for 48 hours ($P<0.05$).
Conclusions: AT1-AA can induce fetal rats' left ventricular hypertrophy and excessive activation of cardiac local RAS may be one of important mechanisms. This study may provide a new strategy and targets for the prevention and treatment of congenital cardiovascular diseases.

GW25-e4226

Vascular Damage Induced by Autoantibodies Against Angiotensin II Type 1 Receptor in Pregnant Rats

Li Hao[1,2], Liu Huirong[1,2]
[1]Department of Physiology and Pathophysiology, Capital Medical University, The Beijing 100069, The People's Republic of China, [2]Beijing Key Laboratory of Cardiovascular Diseases Related to Metabolic Disturbance, Beijing 100069, The People's Republic of China

Objectives: Preeclampsia is a kind of serious pathologic complication during pregnancy. Recent studies have demonstrated that autoantibodies against angiotensin II type 1 receptor (AT1-AA) existed in preeclamptic patients.. In some patients the AT1-AA appears during pregnancy, while some are congenital positive whose AT1-AA appears before pregnancy. As the pathogenesis of preeclampsia is based on systematic vascular damage and increased vascular tension, the roles AT1-AA played in the development of vascular damage in the two types of preeclampsia remain unclear. The present study was designed to determine whether AT1-AA causes vascular damage during pregnancy and the difference between the two types of AT1-AA-positive pregnant rats.
Methods: The model of AT1-AA congenital positive pregnant rats were derived from AT1-AA-positive rats actively immunized with the epitope of the second extracellular loop of angiotensin II type 1 receptor (AT1R), which is the binding epitope of endogenous activating autoantibodies against AT1R from patients with preeclampsia. Another type is made by passively immunizing the pregnant rats with AT1-AA which were generated and purified from AT1-AA actively immunized rats. The titers of AT1-AA were determined by ELISA. Animals were euthanized on day 18 of pregnancy. Endothelin-1 (ET-1) in the sera of rats was determined and vascular cellular adhesion molecule 1 (VCAM-1) expression in the third branch of mesenteric arteries endothelium was assessed using confocal microscopy. The function of resistant arteries was detected in isolated third branch of mesenteric arteries by microvascular ring technique. The expression of vascular smooth muscle α-actin (SM α-actin) was deteced by immunohistochemistry.
Results: The content of ET-1 and vascular endothelial VCAM-1 level were both increased in two types of AT1-AA positive pregnant rats than those of the vehicle group. In addition, mesenteric arteries endothelium-dependent vasodilatation was attenuated in both models, while endothelium-independent vasodilatation and the expression of SM α-actin were decreased in only AT1-AA congenital positive pregnant rats rather than in the passive immunized pregnant rats.
Conclusions: Our study demonstrated that AT1-AA contributed to vascular dysfunction in pregnant rats, while AT1-AA would lead more severe damage in pregnant rats of AT1-AA appearing before pregnancy than that during pregnancy.

GW25-e4292

Systematic analysis of the clinical and biochemical characteristics of maternally inherited hypertension in Chinese Han families associated with mitochondrial genome mutations

Liu Yuqi[1], Chao Zhu[1], Jie Yang[1], Tong Yin[1], Jinliao Gao[1], Zongbin Li[1], Yunfeng Lan[1], Qinghua Ma[5], Yang Li[1], Minxin Guan[2,3,4], Yundai Chen[1], Yundai Chen[1]
[1]Cardiology department, Chinese PLA General Hospital, Beijing, China, [2]Department of Genetics, College of Life Sciences, Zhejiang University, Zhejiang, China, [3]Division of Human Genetics, Cincinnati Children's Hospital Medical Center, Cincinnati, OH, USA, [4]Department of Genetics, College of Life Sciences, Zhejiang University, Zhejiang, China, [5]Department of cardiology, Yishui Center hospital of Shandong Province

Objectives: Hypertension is a very common cardiac vascular disease. Previous studies showed that mitochondrial DNA mutations may be associated with cardiovascular disease, including hypertension.
Methods: In this study we first did segregation analysis and systematically evaluated the whole mitochondrial DNA on 9 maternal inherited hypertension families and the clinical, genetic and molecular characterization of 73 maternal members from these Chinese Han families and 216 healthy controls. In the maternal members, there're 12 members had CHD, 6 with cerebrovascular disease, 5 with diabetes, 9 with hyperlipidemia, 3 with renal disease.
Results: The laboratory test showed that the sodium, potassium level of the maternal members were higher than that of the control group ($P<0.01$), with no difference in FBS, TC, triglyceride, LDL-cholesterol and creatinine ($P>0.05$). While the HDL-cholesterol level of the maternal members was lower than that of the control group ($P=0.04$). Sequence analysis revealed a total of 172 base changes, including 17 in the ribosomal RNA (rRNA) genes, 4 in the transfer RNA (tRNA) genes, and 22 amino acid substitutions, with the remainder involving the noncoding regions or synonymous changes. We identified 7 amino acid changes presented in the 9 maternal inherited hypertension families, including 4 mutations in the ATPase 6, 3 in the Cyt b. More interesting, $tRNA^{Ser\ (UCN)}$ T7492C was identified absent in the controls and <1% in 2704 mtDNAs, with potential functional significance.
Conclusions: This study showed that mtDNA may contribute to the pathogenesis of hypertension in these Chinese Han families due to their structure and function. In the nearly future, more mtDNA mutation could be candidate genes for hypertension.

GW25-e4333

High-resolution Analysis of DNA Copy Number Alterations in Chinese Patients with Isolated Secundum Atrial Septal Defect

Zhao Wei[1], Shen Botao[1], Zheng Yang[1], Li Shibo[2], Zheng Yang[1]
[1]The First Hospital of Jilin University, [2]Department of Pediatrics, OUHSC, Oklahoma City

Objectives: Secundum atrial septal defect (ASD) is the third most common congenital heart malformation and occurs as an isolated defect or as a feature of more complex syndromes. We provide here the submicroscopic imbalances of isolated congenital heart disease (CHD) with a focus on the secundum ASD phenotype, which has not been previously described in detail. We hypothesized that the cases with secundum ASD have specific spectrum of chromosomal imbalance, which might help identify new disease-related loci or genes for ASD.
Methods: A total of 116 Chinese patients with isolated secundum ASD and 340 ethnically matched controls were prospectively screened using whole-genome array comparative genomic hybridization (array-CGH).
Results: A genome-wide survey of 116 isolated secundum ASD patients identified 6 de novo copy number variants (CNVs) that were absent or extremely rare (< 0.1%) in 340 controls. In one of these genomic imbalances (3q21.2), genes known to be associated with heart development were implicated (PLXNA1). Furthermore, recurrent CNVs were also identified at 16q23.1 and 9q22.33.
Conclusions: Although their causal relationship with secundum ASD remains to be established, this CNV profile provides a spectrum of genomic imbalances in this condition, and subsequently improves the CNV-phenotype correlations. Additionally, these findings have potential implications for the genetic counseling of those patients with isolated secundum ASD.

GW25-e4410

The Effects of Lysophosphatidylcholine on action potentials of cardiomyocyets and its mechanisms

Tian Li, Liu Gang, Zheng Mingqi
Department of Cardiology, the 1st Hospital of Hebei Medical Univeristy

Objectives: To explore the effects of LPC on action potentials of cardiomyocytes and its mechanisms.
Methods: Neonatal rat cardiomyocytes from 1 to 3-days Wistar rats were prepared, and the specific Human cardiac T-type calcium channel a1 subunits, Cav3.1 and Cav3.2, were stably expressed in HEK293 cells (HEK293-Cav3.1 and HEK293-Cav3.2). They were incubated for 24h for T-type Ca^{2+} current recording.
Results: LPC (10 mM) or 12-myristate 13-acetate (PMA, 1 mM) markedly accelerated the spontaneous beating rates. $I_{Ca,T}$ was significantly increased by LPC in neonatal cardiomyocytes, which was inhibited by specific Cav3.2 channel blocker, Ni^{2+} (50 mM). Meanwhile, Ni^{2+} completely blocked the effect of LPC on automaticity in spontaneous beating cardiomyocytes.
Conclusions: LPC augmented Cav3.2 channel current to increase the automaticity, which may play a role in triggering arrhythmias in pathophysiological conditions of the heart.

GW25-e4421

Angiotension II upregulates the HCN Channel in Neonatal Rat Cardiomyocytes via a redox mechanism

Wang Le, Zheng Ming-Qi, Liu Gang
Dept. Cardiology, the 1st Hospital, Hebei Medical University